



Review Article

Milk Thistle, Myrrh and Mint: Herbal Plants as Natural Medicines

Mohamad Hesam Shahrajabian^{1*}, Wenli Sun¹, Qi Cheng^{1,2}

1-Biotechnology Research Institute, Chinese Academy of Agricultural Sciences, Beijing 100081, China

2-College of Life Sciences, Hebei Agricultural University, Baoding, Hebei, 071000, China; Global Alliance of HeBAU-CLS&HeQiS for BioAl-Manufacturing, Baoding, Hebei 071000, China

Received: November 2020

Accepted: February 2021

ABSTRACT

Herbs are natural products and herbal medicine has become a popular form of healthcare. Herbal-derived remedies may increase pharmacological qualities and improve prevention and treatment of several diseases. In this study, all relevant articles in English language were collected. Keywords of milk thistle, myrrh, mint and natural products were searched in Google Scholar, Scopus, Research Gate and PubMed databases. Milk thistle is a valuable widely-consumed botanical used for its various health benefits. The plant is an annual herb, belonging to *Asteraceae* family, which ripe seeds contain flavonoid substances. Myrrh is a sap-like substance, which is released from cuts in the barks of trees. The plant is a member of *Commiphora* genus. *Mentha spicata* is a species of mint native to Europe and South-East Asia. Mint is a creeping rhizomatous and perennial herb. In this mini-review, key roles and pharmaceutical benefits of milk thistle, myrrh and mint are described.

Keywords: Milk thistle, Myrrh, Mint, Health benefits, Natural medicine

Introduction

Herbal medications have been reported in Egyptian papyri, traditional Indian, Chinese and Greek Ayurveda and ancient Iranian texts [1–5]. Herbal medicines are types of dietary supplements, which are sold as tablets, capsules, powders, teas, extracts and fresh or dried plants [6–8]. The most important health benefits of herbal medicines include their cost effectiveness, immune system strengthen, less side effects, natural healing potency, hormone and metabolism stabilizing, and affordability, compared to conventional medicines [9–14]. Medicinal plants are potential sources for the development of novel herbal drugs [15–17]. Therefore, herbal plants can be considered as promising medicines for preventing and treating diseases [18–20]. Milk thistle is a flowering plant, which grows in Mediterranean countries and is used to prepare natural remedies. Myrrh is a reddish-brown dried sap from a thorny tree, *Commiphora myrrha*, which is native to Southwest Asia and Northeastern Africa. Mint belongs to the Lamiaceae family, which is a rich-source of polyphenols cultivated in areas with climates ranging from tropical to temperate. The major goal of this study was to review the most important pharmaceutical benefits of milk thistle, myrrh and mint.

Methods

Online databases of ScienceDirect, PubMed, Scopus and Google Scholar were searched using keywords of milk thistle, myrrh, mint, health benefits and natural medicine for articles published between 1970 and 2020.

Results and Discussion

Milk thistle (*Silybummarianum*)

Milk thistle (*S. marianum*) is a valuable widely consumed botanical plant used for its multiple health benefits [21]. It is an annual plant belonging to the Asteraceae family, whose ripe seeds contain flavonoid substances [22]. Milk thistle has been originated from the Mediterranean region and spread to other countries in Europe, Asia, Australia and America. Milk thistle seed oil has been authorized as a novel food resource, which presents a complex unique melting profile [23]. The plant growth criteria are significantly affected by chicken manure and yeast extract. Moreover, the plant silymarin production is enhanced by chicken manure and yeast extract as well [24]. Nitrogen and potassium fertilization and plant spacing significantly affect seed yield and content of the active, antiheptotoxic flavonolignans silybin (silymarin), silidianin and silicristin of *S. marianum* (L.) Gaertn [25]. Milk thistle includes high proteins, fats, flavonolignans and linoleic and oleic acids [26]. The plant

*Address for correspondence: Mohamad Hesam Shahrajabian, Biotechnology Research Institute, Chinese Academy of Agricultural Sciences, Beijing 100081, China. E-mail address: hesamshahrajabian@gmail.com

primary extract is termed silymarin, a complex mixture that contains a number of structurally linked flavonolignans, flavonoids, taxifolin and other constituents. The major flavonolignans present in most extracts include silybin A, silybin B, isosilybin A and isosilybin B, silydianin, silychristin and isosilychristin [27,28]. The most important therapeutic uses of silymarin include their anti-diabetes, anti-dermatitis, anti-cancer, anti-Alzheimer, anti-Parkinson and hepatoprot-

ective uses [29]. Silymarin derived from the milk thistle plant has been used as a natural remedy for diseases of the liver and biliary tract [30–32], which appears to be safe and well tolerated [33,34]. The seeds are promising natural drugs [35]. Milk thistle botanical supplements were reported to include a wide variety of fungal species. The most important pharmaceutical benefits of milk thistle are shown in Table 1.

Table 1. Pharmaceutical benefits of milk thistle

Benefit	Mechanism and impact	Reference
Antioxidant activity	a. Milk thistle syrup has high antioxidant activity. b. The films with milk thistle extract has shown higher antioxidant activities and lower solubility. c. The bioactive properties were positively correlated with phenolics/flavonoids content.	[36-42]
Anti-cancer	a. Silymarin and a flavonoid antioxidant isolated from milk thistle have shown the cancer chemopreventive and anti-carcinogenic effects. b. Silymarin has anti-cancer activity in human breast cancer, skin cancer, colon cancer, cervical cancer, prostate cancer, ovarian cancer, bladder cancer and lung cancer cells.	[43-47]
Liver protective effects	a. Milk thistle appears to be relatively safe, with long-term use for its potentially protective effects on the liver.	[48-50]
Anti-diabetic activity	a. The potent hypoglycaemic and antihyperglycaemic activities of an aqueous extract of milk thistle have also been demonstrated animal models of diabetes.	[51]
Anti-melanogenesis	a. Milk thistle has a potent potential to tyrosinase inhibition.	[52]
Anti-carcinogenic	a. The silymarin compounds are anticarcinogenic substances.	[53]
Hepatoprotective effects	a. Silibin, a flavinoligand derived from milk thistle, is a dietary supplement reported to exert hepatoprotective.	[54-56]
Antiviral effects	a. Silymarin flavonolignans had antiviral effects.	[57-60]
Anti-inflammatory effects	a. Anti-inflammatory effects of silymarin are related to inhibition of the transcription factor nuclear factor- κ B (NF- κ B), which regulates and coordinates the expression of various genes involved in inflammation, cell survival, differentiation and growth.	
Anti-aflatoxin activity	a. It has beneficial properties of milk thistle on poultry growth performance in experimentally induced aflatoxicosis.	[61]

Myrrh (*Commiphora* spp.)

The Genus includes nearly 190 species and is distributed in Southern Arabia (Yemen and Oman), Northeastern Africa (Somalia, Ethiopia and Sudan) and Subcontinent (India and Pakistan) [62,63]. Myrrh is a natural gum or resin extracted from a number of small, thorny tree species of the *Commiphora* genus. It is an herbal product, which has been used since ancient ages for traditional medications and other purposes [64,65]. The most important species of myrrh are *C.africana*, *C.angolensis*, *C.boranensis*, *C. caudate*, *C.erythrae*, *C.gileadensis*, *C.glandulosa*, *C.guidottii*, *C.guillaminii*, *C.habessinica*, *C.harveyi*, *C.holtziana*, *C.humbertii*, *C.kataf*, *C.madagascariensis*, *C.mossambicensis*, *C.myrrha*, *C.schimperi*, *C.simplicifolia*, *C.sphaerocarpa*, *C.stocksiana* and *C.wightii*. Since ancient eras, the plant has been used as a medicine and wound dressing, closely linked to the health and purification of rituals of women. Furthermore, the herbal was first described in Chinese medical literatures. The first use of myrrh was recorded in China during Tang Dynasty [66]. Traditional uses of *C. molmol* for the treatment of pain, inflammation and hyperlipidemia have been recorded [67]. Traditional use of *C. molmol* as a poultice for the treatment of cutaneous fungal infections has also been suggested [68]. Myrrh is an effective anti-microbial agent, which is reported as an excellent external remedy for mouth, throat and skin infections as well as glandular fever and brucellosis [69]. Myrrh essential oil is a promising antibacterial and cytotoxic agent [70]. Myrrh extract can be used alone or in combination with sublethal doses of certain insecticides to control cotton leaf worms [71]. It shows antimicrobial

properties on wool and silk fabrics [72]. Furthermore, myrrh essential oil includes potentials to qualify as an alternative of synthetic fungicides, particularly managing post-harvest fungal infections [73]. The oil of *C.kua* has shown moderate antifungal activities against *Cladosporium cucumerinum* [74]. Antibacterial and anti-inflammatory activities of myrrh are suggested based on the results from several studies. Moreover, anti-inflammatory activity of dual combination of myrrh and chamomile is reported⁷⁵. Myrrh provides novel indications for itch treatment, which cannot be treated with histamine receptor blockers alone⁷⁶. Hard gelatin capsules of myrrh extract are effective as pharmaceutical dosages against schistosomiasis⁷⁷. Myrrh helps maintain increased levels of white blood cells (WBC) through the healing period⁷⁸. The native myrrh use for severe vulvar edema in ovarian hyperstimulation syndrome may result in substantial improvement [79].

Mint (*Mentha* spp.)

Mint (*Mentha* spp.) includes diverse uses, including pharmaceutical, perfumery, food and confectionery uses [80,81]. The *M.spicata* is a species of mint native to Europe and South-East Asia [82]. The major essential oil of *M.spicata* L. includes piperitenone oxide, carvone, limonene, 1,8-cineole, menthone and isomenthone [83,84]. Kofidis et al. [85] reported that the essential oil from the leaves of *M.spicata* included high contents of linalool. The *M.spicata* can improve lipid profile of blood, meat quality and microbial population in small intestine [86]. The herbal oil can decrease pains in osteoarthritis patients [87]. The most significant pharmaceutical benefits of mint are presented in Table 2.

Table 2.Pharmaceutical benefits of mint

Benefit	Mechanism and impact	Reference
Antimicrobial activity	a. <i>M. spicata</i> essential oil can be considered as a natural source of bioactive phytochemicals bearing antimicrobial activities. b. The recovered and decanted essential oils of <i>Mentha</i> species demonstrated low to moderate antimicrobial activity against five bacterial strains. c. The oil showed great potential for its antimicrobial activities against <i>Escherichia coli</i> , <i>Candida albicans</i> , <i>Candida tropicalis</i> and moderate activities against <i>Staphylococcus aureus</i> .	[88-92]
Anti-bacterial	a. <i>M. spicata</i> essential oil has antibacterial activities.	[93-95]
Antibiotics	a. High total antioxidant activity in <i>M. Spicata</i> (79-85%) has proved the possible use of <i>Mentha</i> oils as alternative antibiotics.	
Anti-fungal activity	a. The extract of <i>mentha spicata</i> L. completely inhibited the mycelia growth of the pathogen.	[96,97]
Anti-inflammatory	a. Two monoterpenoid glycosides, spicatoside A and spicatoside B isolated from the whole plant has shown anti-inflammatory and hemostatic activity.	[98,99]
Antioxidant activity	a. S-Carvone isolated from <i>Menthaspicata</i> possess high antioxidant activity compared to α -tocopherol. The aqueous fraction of <i>M. spicata</i> mediates their antigenotoxic effects by modulation of lipid peroxidation (LPO) and antioxidant enzymes.	[100-105]
Anticarcinogenic properties	a. Piperitenone oxide is the first potential medical benefits of anticarcinogenic properties.	[106]
Pesticide	a. <i>M. spicata</i> essential oil is recommended as plant based pesticide.	[107]

Conclusions

The most health benefits of milk thistle support liver health, promote skin health, decrease cholesterol, support weight loss, decrease insulin resistance, improve allergic asthma symptoms, limit spread of cancers and support bone health. The most significant benefits of myrrh oil include killing harmful bacteria, supporting oral and skin health and healing sores. The plant includes powerful antioxidant characteristics, which fight oxidative damages and kill parasites. Moreover, the herb may help kill or slow the growth of cancer cells. Myrrh compounds may help treat intestinal spasms linked to irritable bowel syndrome (IBS) as well as killing molds. The most important health benefits of mint include its goodness for digestive upsets, high antioxidant contents, memory improvement, popularity in toothpaste flavoring, breath mints and chewing gums, blood sugar decrease properties, stress reduction power, relaxation promotion and joint pain relieve due to arthritis. In conclusion, traditional medicine herbs play important roles in sustainable agriculture and food systems. They also offer significant approaches to prevent diseases.

Acknowledgement

Not applicable.

Authors' Contribution

All authors contributed equally to searching literatures and writing the manuscript.

Funding/Support

This study was supported by the National Key R&D Program of China (research grant: 2019YFA0904700)

Availability of data and materials

Not applicable.

Ethics approval and consent to participate

Not applicable.

Consent for publication

The authors consent for the publication of this review.

Financial disclosure

The authors declare no competing interests.

References

- Ogbaji PO, Li J, Xue X, Shahrajabian MH, Egrinya EA. Impact of Bio-fertilizer or nutrient solution on Spinach (*Spinaciaeoleracea*) growth and yield in some province soils of P.R. China. *CercetariAgronomice in Moldova*. 2018; 51(2): 43-52.
- Soleymani A, Shahrajabian MH. Changes in germination and seedling growth of different cultivars of cumin to drought stress. *CercetariAgronomice in Moldova*. 2018; 51(1): 91-100.
- Sun W, Shahrajabian MH, Cheng Q. Anise (*Pimpinellaanisum* L.), a dominant spice and traditional medicinal herb for both food and medicinal purposes. *Cogent Biol*. 2019; 5(1673688): 1-25.
- Sun W, Shahrajabian MH, Cheng Q. Therapeutic roles of goji berry and ginseng in traditional Chinese. *J Nutr Food Secur*. 2019; 4(4): 293-305.
- Sun W, ShahrajabianMH, Cheng Q. The insight and survey on medicinal properties and nutritive components of shallot. *J Med Plant Res*. 2019; 13(18): 452-457.
- Sun W, Shahrajabian MH, Cheng Q. Pyrethrum and organic and natural pesticide. *J Biol Environ Sci*. 2020; 14(40): 41-44.
- Sun W, Shahrajabian MH, Khoshkham M, Shen H, Cheng Q. Cultivation of cotton in China and Iran with considering biological activities and its health benefits. *CercetariAgronomice in Moldova*. 2020; 1(181): 105-120.
- Sun W, Shahrajabian MH, Khoshkham M, Cheng Q. Adaptation of acupuncture and traditional Chinese herbal medicines models because of climate change. *J Stress PhysiolBiochem*. 2020; 16(1): 85-90.
- Shahrajabian MH, Sun W, Cheng Q. Clinical aspects and health benefits of ginger (*Zingiberofficinale*) in both traditional Chinese medicine and modern industry. *ActaAgricScand, Sec B- Soil Plant Sci*. 2019. DOI: 10.1080/09064710.2019.1606930
- Shahrajabian MH, Sun W, Cheng Q. A review of ginseng species in different regions as a multipurpose herb in traditional Chinese medicine, modern herbology and pharmacological science. *J Med Plant Res*. 2019; 13(10): 213-226.
- Shahrajabian MH, Sun W, Cheng Q. DNA methylation as the most important content of epigenetics in traditional Chinese herbal medicine. *J Med Plant Res*. 2019; 13(16): 357-369.
- Shahrajabian MH, Sun W, Cheng Q. A review of astragalus species as foodstuffs, dietary supplements, a traditional Chinese medicine and a part of modern pharmaceutical science. *ApplEcol Environ Res*. 2019; 17(6): 13371-13382.
- Shahrajabian MH, Sun W, Zandi P, Cheng Q. A review of chrysanthemum, the eastern queen in traditional Chinese medicine with healing power in modern pharmaceutical sciences. *ApplEcol Environ Res*. 2019; 17(6): 13355-13369.
- Shahrajabian MH, Sun W, Cheng Q. Tremendous health benefits and clinical aspects of *Smilax china*. *African J Pharm Pharmacol*. 2019; 13(16): 253-258.
- Shahrajabian MH, Sun W, Cheng Q. Traditional herbal medicine for the prevention and treatment of cold and flu in the Autumn of 2020, overlapped with COVID-19. *Nat Prod Commun*. 2020; 15(8): 1-10.
- Shahrajabian MH, Sun W, Cheng Q. Product of natural evolution (SARS, MERS, and SARS-CoV-2); deadly diseases, from SARS to SARS-CoV-2. *Human Vaccine Immunother*. 2020. DOI: 10.1080/21645515.2020.1797369
- Shahrajabian MH, Sun W, Cheng Q. Chinese onion and shallot, originated in Asia, medicinal plants for healthy daily recipes. *NotSci Biol*. 2020; 12(2): 197-207.
- Shahrajabian MH, Sun W, Cheng Q. Considering white gold, cotton for its fiber, seed oil, traditional and modern health benefits. *J Biol Environ Sci*. 2020; 14(40): 25-39.

19. Shahrajabian MH, Sun W, Shen H, Cheng Q. Chinese herbal medicine for SARS and SARS-CoV-2 treatment and prevention, encouraging using herbal medicine for COVID-19 outbreak. *ActaAgricScand, Sec B- Soil Plant Sci.* 2020. DOI: 10.1080/09064710.2020.1763448
20. Shahrajabian MH, Sun W, Cheng Q. Chinese star anise (*Illiciumverum*) and pyrethrum (*Chrysanthemum cinerariifolium*) as natural alternatives for organic farming and health care- A review. *Aust J Crop Sci.* 2020; 14(03): 517-523.
21. Hammami H, Saadatian B, Hosseini SAH. Geographical variation in seed germination and biochemical response of milk thistle (*Silybummarianum*) ecotypes exposed to osmotic and salinity stresses. *Industrial Crops and Products* 2020; 152: 112507.
22. Ghavami N, Ramin AA. Salinity and temperature effects on seed germination of milk thistle. *Commun Soil Sci Plant Anal.* 2007; 38(19-20): 2681-2691.
23. Zhang Z-S, Wang S, LiuH, Li B-Z, Che L. Constituents and thermal properties of milk thistle seed oils extracted with three methods. *LWT.* 2020; 126: 109282.
24. Saad-Allah K, Fetouh MI, Elhaak MA. Induction of milk thistle (*Silybummarianum* L. Gaertn) growth and phytochemicals production by natural stimulants. *J Appl Res Med Aroma.* 2017; 6: 101-110.
25. Omer EA, Refaat AM, Ahmed SS, Kamel A, Hammouda FM. Effect of spacing and fertilization on the yield and active constituents of milk thistle, *Silybummarianum*. *J Herbs Spices Med Plants.* 1993; 1(4): 17-23.
26. Grela ER, Swiatkiewicz M, Florek M, Wojtaszewska I. Impact of milk thistle (*Silybummarianum* L.) seeds in fattener diets on pig performance and carcass traits and fatty acid profile and cholesterol of meat, backfat, and liver. *Livest Sci.* 2020; 239: 104180.
27. Albassam AA, Frye RF, Markowitz JS. The effect of milk thistle (*Silybummarianum*) and its main flavonolignans on CYP2C8 enzyme activity in human liver microsomes. *ChemBiol Interact.* 2017; 271: 24-29.
28. Lee JI, Hsu BH, Wu D, Barrett JS. Separation and characterization of silybin, isosilybin, silydianin and silychristin in milk thistle extract by liquid chromatography-electrospray tandem mass spectrometry. *J Chromatogr A.* 2006; 1116(1-2): 57-68.
29. Soleimani V, Delghandi PS, MoallemSA, Karimi G. Safety and toxicity of silymarin, the major constituents of milk thistle extract: An updated review. *Phytother Res.* 2019; 1-12.
30. Flora MDK, Hahn MDM, Rosen MDH, Benner MDK. Milk thistle (*Silybummarianum*) for the therapy of liver disease. *Am J Gastroenterol.* 1998; 93(2): 139-143.
31. Jedlinski N, Kalomista I, Galbacs G, Csupor D. *Silybummarianum* (milk thistle) products in Wilson's disease: a treatment of a threat? *J Herb Med.* 2016; 6(3): 157-159.
32. Karkanis A, Bilalis D, Efthimiadou A. Cultivation of milk thistle (*Silybummarianum* L. Gaertn), a medicinal weed. *Ind Crops Prod.* 2011; 34(1): 825-830.
33. Jacobs BP, Dennehy C, Ramirez G, Sapp J, Lawrence VA. Milk thistle for the treatment of liver disease: A systematic review and meta-analysis. *Am J Med.* 2002; 113(6): 506-515.
34. Ceribasi S, Turk G, Ozcelik M, Dogan G, Ceribasi AO, Mutlu SI, Erisir Z, Guvenc M, Gungoren G, Acisu TC, Akarsu SA, Kaya SO, Sonmez M, Yuce M, Yuce A, Ciftci M, Cambay Z, Bagci E, Azman MA, Simsek UG. Negative effect of feeding with high energy diets on testes and metabolic blood parameters of male Japanese quails, and positive role of milk thistle seed. *Theriogenology.* 2020; 144: 74-81.
35. Bhattacharya S. Milk thistle seeds in health. In book: *Nuts and seeds in health and disease prevention.* 2020; 429-438.
36. Zheng X, Wang X, Lan Y, Shi J, Xue SJ, Liu C. Application of response surface methodology to optimize microwave-assisted extraction of silymarin from milk thistle seeds. *Sep Purif Technol.* 2009; 70(1): 34-40.
37. Vaknin Y, Hadas R, Schafferman D, Murkhovskiy L, Bashan N. The potential of milk thistle (*Silybummarianum* L.), an Israeli native, as a source of edible sprouts rich in antioxidants. *Int J Food Sci Nutr.* 2008; 59(4): 339-346.
38. Pereira C, Calhelha RC, Barros L, Ferreira ICFR. Antioxidant properties, anti-hepatocellular carcinoma activity and hepatotoxicity of artichoke, milk thistle and borututu. *Ind Crops Prod.* 2013; 49: 61-65.
39. Pereira C, Calhelha RC, Barros L, Queiroz MJRP, Ferreira ICFR. Synergisms in antioxidant and anti-hepatocellular carcinoma activities of artichoke, milk thistle and borututu syrups. *Ind Crops Prod.* 2014; 52: 709-713.
40. Ghelejlou SB, Esmaili M, Almasi H. Characterization of chitosan-nanoclay-bionanocomposite active films containing milk thistle extract. *Int J Biol Macromol.* 2016; 86: 613-621.
41. Attia YA, Hamed RS, Bovera F, El-Hamid AEHEA, Al-Harthi MA, Shahba HA. Semen quality, antioxidant status and reproductive performance of rabbits bucks fed milk thistle seeds and rosemary leaves. *Anim Reproduct Sci.* 2017; 184: 178-186.
42. Lucini L, Kane D, Pellizzoni M, Ferrari A, Trevisi E, Ruzickova G, Arslan D. Phenolic profile and in vitro antioxidant power of different milk thistle (*Silybummarianum* (L.) Gaertn.) cultivars. *Ind Crops Prod.* 2016; 83: 11-16.
43. Bhatia N, Zhao J, Wolf DM, Agrawal R. Inhibition of human carcinoma cell growth and DNA synthesis by silybinin, an active constituent of milk thistle: comparison with silymarin. *Cancer Lett.* 1999; 147(1-2): 77-84.
44. Singh RP, Agarwal R. Mechanisms and preclinical efficacy of silybinin in preventing skin cancer. *Eur J Cancer.* 2005; 41: 1969-1979.
45. Sing RP, Agarwal R. Prostate cancer chemopreventive by silybinin: bench to bedside. *Mol Carcinog.* 2005; 45(6): 436-442.
46. Lin A-S, Shibano M, Nakagawa-Goto K, Tokuda H, Itokawa H, Morris-Natschke SL, Lee K-H. Cancer preventive agents. 7. Antitumor-promoting effects of seven active flavonolignans from milk thistle (*Silybummarianum*) on Epstein-Bar virus activation. *Pharm Biol.* 2007; 54(10): 735-738.
47. Mohaghegh F, Solhi H, Kazemifar AM. Silymarin (Milk Thistle) can revoke liver enzyme changes during chemotherapy of breast cancer with Taxanes. *Eur J Integr Med.* 2015; 7(6): 650-652.

48. Abenavoli L, Bellentani S. Milk thistle to treat non-alcoholic fatty liver disease: dream or reality? *Expert Rev GastroenterolHepatol*. 2013; 7(8): 677-679.
49. Li ZX, Li M, Huang XS, Liang HM, Li JL, Huang XH. Study on the bacteriostatic effect of cinnamon oil on acne-inducing bacteria. *Guangdong Pharm Univ*. 2018; 34: 719-723.
50. Boerth J, Strong KM. The clinical utility of milk thistle (*Silybummarianum*) in cirrhosis of the liver. *J Herb Pharmacother*. 2002; 2(2): 11-17.
51. Maghrani M, Zeggwagh NA, Lemhadri A, El Amraoui M, Michel JB, Eddouks M. Study of the hypoglycaemic activity of *Fraxinus excelsior* and *Silybummarianum* in an animal model of type 1 diabetes mellitus. *J Ethnopharmacol*. 2004;91: 309-316.
52. Kim JY, Kim JY, Jenis J, Li ZP, Ban YJ, Baiseitova A, Park KH. Tyrosinase inhibitory study of flavonolignans from the seeds of *Silybummarianum* (Milk thistle). *Bioorg Med Chem*. 2019; 27(12): 2499-2507.
53. Celik HT, Guru M. Extraction of oil and silybin compounds from milk thistle seeds using supercritical carbon dioxide. *J Supercrit Fluids*. 2015;100: 105-109.
54. Jancova P, Siller M, Anzenbacherova E, Kren V, Anzenbacher P, Simanek V. Evidence for differences in regioselective and stereoselective glucuronidation of silybindiastereomers from milk thistle (*Silybummarianum*) by human UDP-glucuronosyltransferases. *Xenobiotica*. 2011; 41(9): 743-751.
55. Brandon-Warner E, Eheim AL, Foureau DM, Walling TL, Schrum LW, McKillop IH. Silibinin (Milk Thistle) potentiates ethanol-dependent hepatocellular carcinoma progression in male mice. *Cancer Lett*. 2012; 326(1): 88-95.
56. El-Gazayerly ON, Makhlof AIA, Soelm AMA, Mohmoud MA. Antioxidant and hepatoprotective effects of silymarin phytosomes compared to milk thistle extract in CCl₄ induced hepatotoxicity in rats. *J Microencapsul*. 2014; 31(1): 23-30.
57. Althagafy HS, Graf TN, Sy-Cordero AA, Gufford BT, Paine MF, Wagoner J, Polyak SJ, Croatt MP, Oberlies NH. Semisynthesis, cytotoxicity, antiviral activity, and drug interaction liability of 7-O-methylated analogues of flavonolignans from milk thistle. *Bioorg Med Chem*. 2013; 21(13): 3919-3926.
58. Bhattacharya S. Milk thistle (*Silybummarianum* L. Gaert.) seeds in health. In book: *Nuts and Seeds in Health and Disease Prevention*. 2011; 759-766.
59. Fanoudi S, Alavi MS, Karimi G, Hosseinzadeh H. Milk thistle (*SilybumMarianum*) as an antidote or a protective agent against natural or chemical toxicities: a review. *Drug Chem Toxicol*. 2020; 43(3): 240-254.
60. Ramasany K, Agrarwal R. Mutitargeted therapy of cancer by silymarin. *Cancer Lett*. 2008; 269(2): 352-362.
61. Alhidary IA, Rehman Z, Khan RU, Tahir M. Anti-aflatoxin activities of milk thistle (*Silybummarianum*) in broiler. *Worlds PoultSci J*. 2017; 73(3): 559-566.
62. Shen T, Li GH, Wang X-N, Lou H-X. The genus *Commiphora*: a review of its traditional uses, phytochemistry and pharmacology. *J Ethnopharmacol*. 2012; 142: 319-330.
63. Weeks A, Simpson BB. Molecular phylogenetic analysis of *Commiphora* (Burseraceae) yields insight on the evolution and historical biogeography of an impossible genus. *MolPhylogenetEvol*. 2007; 42: 62-79.
64. Alqahtani AS, Noman OM, RehmanMdT, Siddiqui NA, Alajmi MF, Nasr FA, Shahat AA, Alam P. The influence of variations of furanosesquiterpenoids content of commercial samples of myrrh on their biological properties. *Saudi Pharm J*. 2019;27: 981-989.
65. Abdul-Hamid M, Gallaly SR. Ameliorative effect of *Pimpinellaanisum* oil on immunohistochemical and ultrastructural changes of cerebellum of albino rats induced by aspartame. *UltrastructPathol*. 2014; 38(3): 224-236.
66. Hanus LO, Rezanka T, Dembitsky VM, Moussaieff A. Myrrh- *Commiphora* chemistry. *Biomed Papers*. 2005; 149(1): 3-28.
67. Shalaby MA, Hammouda AA-E. Analgesic, anti-inflammatory and anti-hyperlipidemic activities of *Commiphoramolmol* extract (Myrrh). *J IntercultEthnopharmacol*. 2014; 3(2): 56-62.
68. Mahboubi M, Kashani LMT. The anti-dermatophyte activity of *Commiphoramolmol*. *Pharma Biol*. 2016; 54(4): 720-725.
69. Abdel-Hay MH, Saleh A, El Ashry ESH, Rashed N, Salama O. Colorimetric determination of crude powdered myrrh, purified myrrh extract, oily fraction, and its different pharmaceutical dosage forms. *Spectrosc Lett*. 2002; 35(2): 183-197.
70. Khalil N, Fikry S, Salama O. Bactericidal activity of myrrh extracts and two dosage forms against standard bacterial strains and multidrug-resistant clinical isolates with GC/MS profiling. *AMB Express*. 2020;10(21): 1-10.
71. Shonouda ML, Farrag RM, Salama OM. Efficacy of the botanical extract (myrrh), chemical insecticides and their combinations on the cotton leafworm, *Spodopteralittoralis*boisd (Lepidoptera: Noctuidae). *J Environ Sci Health, Part B*. 2000; 35(3): 347-356.
72. Salem AA, Al moudi HA. Application of myrrh extract as an eco-friendly dye and antimicrobial agent on wool and silk fabrics part 2: antimicrobial activity and fastness property. *J Nat Fibers*. 2020;17(4): 491-504.
73. Perveen K, Bokhari N, Siddique I, Al-Rashid SA. Antifungal activity of essential oil of *Commiphoramolmol* Oleo gum resin. *Journal of Essential Oil Bearing Plants* 3(21): 667-673.
74. Ali NAA, Wurster M, Arnold N, Lindequist U, Wessjohan L (2008) Essential oil composition from Oleogum resin of soqotraen *Commiphorakua*. *Rec Nat Prod*. 2018; 2(3): 70-75.
75. Vissienon C, Hammoud D, Goos K-H, Nieber K, Arnhold J. Synergistic interactions of chamomile flower, myrrh and coffee charcoal in inhibiting pro-inflammatory chemokine release from activated human macrophages. *Synergy*. 2017; 4: 13-18.
76. Shin W-Y, Shim D-W, Kim M-K, Sun X, Koppula S, Yu S-H, Kim H-B, Kim TJ, Kang T-B, Lee K-H. Protective effects of *Cinnamomum cassia* (Lamaceae) against gout and septic responses via attenuation of inflammasome activation in experimental models. *J Ethnopharmacol*. 2017; 205: 173-177.
77. Hashem FM, Massoud AMA, Melokheya AM, Emad H, El-Fattah Badr KA, Dawoud M. Formulation and clinical efficacy of myrrh extract in hard gelatin capsules. *JBiol Active Prod Nat*. 2013; 3(1): 72-86.

78. Haffor A-SA. Effect of myrrh (*Commiphoramolmol*) on leukocyte levels before and during healing from gastric ulcer or skin injury. *J Immunotoxicol*. 2010; 7(1): 68-75.
79. Hijazi A, Al-Jaroudi D. Myrrh for treatment of severe vulvar edema in ovarian hyperstimulation syndrome. *Case Rep Women's Health*. 2017; 15: 8-10.
80. Zeinali H, Razmjo K, Arzani A. Diversity among Iranian mints in relation to yield and mineral content. *CommunSoil Sci Plant Anal*. 2003; 34(15-16): 2203-2217.
81. Prasad A, Singh AK, Chand S, Chanotiya CS, Patra DD. Effect of chromium and lead on yield, chemical composition of essential oil, and accumulation of heavy metals of mint species. *CommunSoil Sci Plant Anal*. 2010; 41(18): 2170-2186.
82. Samantaray A, Sial P, Kar M. Micro-propagation and biochemical analysis of Spear Mint (*Menthaspicata*). *Indian J Innovations Dev*. 2010; 1(7): 489-493.
83. Younis YMH, Beshir SM. Carvone-rich essential oils from *Menthalongifolia* (L.) Huds. ssp. schimperibriq. And *Menthaspicata* L. grown in Sudan. *J Essent Oil Res*. 2004; 16(6): 539-541.
84. Chauhan RS, Nautiyal MC, Tava A. Essential oil composition from aerial parts of *Menthaspicata* L. *J Essent Oil-Bear Plants*. 2010; 13(3): 353-356.
85. Kofidis G, Bosabalidis A, Kokkini S. Seasonal variation of essential oils in a linalool-rich chemotype of *Menthaspicata* grown wild in Greece. *J of Essent Oil Res*. 2004; 16(5): 469-472.
86. Ghazaghi M, Mehri M, Bagherzadeh-Kasmani F. Effects of dietary *Menthaspicata* on performance, blood metabolites, meat quality and microbial ecosystem of small intestine in growing Japanese quail. *Anim Feed Sci Technol*. 2014; 194: 89-98.
87. Mahboubi M. *Menthaspicata* as natural analgesia for treatment of pain in osteoarthritis patients. *Complement TherClinPract*. 2017; 26: 1-4.
88. Hussain AI, Anwar F, Shahid M, Ashraf M, Przybylski R. Chemical composition, and antioxidant and antimicrobial activities of essential oil of spearmint (*Menthaspicata* L.) from Pakistan. *JEssent Oil Res*. 2010; 22(1): 78-84.
89. Sharafi SM, Rasooli I, Owlia P, Nadoushan MJ, Ghazanfari T, Taghizadeh M. Phytochemical bioactives from *Menthaspicata* essential oil for health promotion. *J Essent Oil-Bear Plants*. 2010; 13(2): 237-249.
90. Sarer E, Toprak SY, Otlu B, Durmaz R. Composition and antimicrobial activity of the essential oil from *Menthaspicata* L. subsp. *Spicata*. *J Essent Oil Res*. 2011; 23(1): 105-108.
91. Verma RS, Pandey V, Padalia RC, Saikia D, Krishna B. Chemical composition and antimicrobial potential of aqueous distillate volatiles of Indian peppermint (*Menthapiperita*) and spearmint (*Menthaspicata*). *J of Herbs Spices Med Plants*. 2010; 17(3): 258-267.
92. Chrysargyris A, Xylia P, Botsaris G, Tzortzakis N. Antioxidant and antibacterial activities, mineral and essential oil composition of spearmint (*Menthaspicata* L.) affected by the potassium levels. *Ind Crops Prod*. 2017; 103: 202-212.
93. Scherer R, Lemos MF, Lemos MF, Martinelli GC, Martins JDL, Silva AGD. Antioxidant and antibacterial activities and composition of Brazilian spearmint (*Menthaspicata* L.). *Ind Crops Prod*. 2013; 50: 408-413.
94. Shahbazi Y, Shavisi N. Interactions of *Ziziphoraclinopodioides* and *Menthaspicata* essential oils with chitosan and ciprofloxacin against common food-related pathogens. *LWT-Food Sci Technol*. 2016; 71: 364-369.
95. Elansary HO, Ashmawy NA. Essential oils of mint between benefits and hazards. *J Essent Oil Bear Plants*. 2013; 16(4): 429-438.
96. Singh J, Dubey AK, Tripathi NN. Antifungal activity of *Menthaspicata*. *Int J Pharmacog*. 1994; 32(4): 314-319.
97. Bayan Y, Kusek M. Chemical composition and antifungal and antibacterial activity of *Menthaspicata* L. volatile oil. *Ciencia e InvestigacionAgararia*. 2018; 45(1): 64-69.
98. Zheng J, Wu L-J, Zheng L, Wu B, Song A-H. Two new monoterpenoid glycosides from *Menthaspicata* L. *Journal of Asian Natural Products Research*. 2003; 5(1): 69-73.
99. Arumugam P, Priya NG, Subathra M, Ramesh A. Anti-inflammatory activity of four solvent fractions of ethanol extract of *Menthaspicata* L. investigated on acute and chronic. *EnvironToxicolPharmacol*. 2008; 26(1): 92-95.
100. Arumugam P, Ramesh A. Antigenotoxic and antioxidant potential of aqueous fraction of ethanol extract of *Menthaspicata* (L.) against 4-nitroquinoline-1-oxide-induced chromosome damage in mice. *DrugChemToxicol*. 2009; 32(4): 411-416.
101. Arumugam P, Ramamurthy P, Ramesh A. Antioxidant and cytotoxic activities of lipophilic and hydrophilic fractions of *MenthaSpicata* L. (Lamiaceae). *Int J Food Prop*. 2010; 13(1): 23-31.
102. Elmastas M, Dermirtas I, Isildak O, Aboul-Enein HY. Antioxidant activity of S-carvone isolated from spearmint (*MenthaSpicata* L. *FamLamiaceae*). *J LiqChromatogrRelta Technol*. 2006; 29(10): 1465-1475.
103. Wang D, Chen X, Wang Q, Meng Y, Wang D, Wang X. Influence of the essential oil of *Menthaspicata* cv. *Henanshixiang* on sunflower oil during the deep-frying of Chinese *Maye*. *LWT*. 2011; 122: 109020.
104. Mandana B, Russly AR, Ali G, Farah ST. Antioxidant activity of spearmint (*Menthaspicata* L.) leaves extracts by supercritical carbon dioxide (SC-CO₂) extraction. *IntFood Res J*. 2011; 18: 543-547.
105. Chrysargyris A, Petropoulos SA, Fernandes A, Barros L, Tzortzakis N, Ferreira ICFR. Effect of phosphorus application rate on *Menthaspicata* L. grown in deep flow technique (DFT). *Food Chem*. 2019; 276: 84-92.
106. Nakamura Y, Hasegawa Y, Shiota K, Suetome N, Nakamura T, Chomnawang MT, Thirapanmethee K, Khuntayaporn P, Boonyariththongchai P, Wongs-Aree C, Okamoto S, Shigeta T, Matsu T, Park EY, Sato K. Differentiation-inducing effects of piperitenone oxide, a fragrant ingredient of spearmint (*Menthaspicata*), but not carvone and menthol, against human colon cancer cells. *J Funct Foods*. 2014; 8: 62-67.
107. Kedia A, Prakash B, Mishra PK, Chanotiya CS, Dubey NK. Antifungal, antiaflatoxicogenic, and insecticidal efficacy of spearmint (*Menthaspicata* L.) essential oil. *IntBiodeterBiodegr*. 2014; 89: 29-36.